It is common, in talking about higher education, to distinguish between teaching and research, and to argue that the two activities are somehow in conflict. No one who understands either teaching or research, however, believes that the two are opposed to each other. The purpose of a university is to lead superior intelligence to do its best, whether in the classroom or the laboratory. In both venues, professors and students in a great university must and do excel.

Because external funding for research is in finite supply, this funding provides a clear and reliable benchmark of the intellectual excellence of a university. By this benchmark, Boston University excels. In 1971, the University received $15 million in grants and contracts supporting its research. In 2002/2003 the University’s annual receipt for sponsored research was just over $311 million. In constant dollars—that is, in real money—funding more than quadrupled.

The University’s research funding is not only growing; it is growing intelligently, as recent grants support work that will put the University at the forefront of several disciplines. In biomedical engineering, our $14 million leadership grant from the Whitaker Foundation, for example, is allowing the University to integrate ground-breaking research in genomics, cellular engineering, and physiology. Our $20 million National Science Foundation grant to investigate space weather allows our astronomers, electrical engineers, and computer scientists to collaborate on developing far more sophisticated models of the solar system than we now know.

This publication details some of the many scientific insights and opportunities that Boston University’s classrooms and laboratories are generating today. I hope you will find it as exciting as I do.

John Silber
Research at Boston University 2003

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Research in Tejal Desai’s Therapeutic Microtechnology Laboratory uses the methods and materials of MEMS (microelectromechanical systems) to create implantable biological devices that hold the potential to cure diabetes, create intelligent oral delivery systems for targeted cancer treatment, and produce templates for cell and tissue regeneration.
Beginning with the Basics

Understanding Disease at the Most Primary Levels

With the support of a $14-million Leadership Grant from the Whitaker Foundation, Boston University scientists are probing deeply into the very nature of how life conducts itself—investigating how genes control the complex folding and functioning of proteins, how proteins impact the growth and vitality of cells, and what happens when things do not go according to plan.

Beyond Genomics

Boston University faculty members were among the international team of scientists who broke the news in early 2001 that they had completed mapping the entire human genome. This momentous project was, in fact, kicked off by Charles DeLisi, then at the U.S. Department of Energy, “Just as Lewis and Clark set forth to explore a continent shrouded in mysterious possibility, Charles DeLisi pioneered the exploration of a modern-day frontier, the human genome,” President Clinton said when he presented DeLisi with the Presidential Citizen’s Medal.

Now Senior Associate Provost for Bioinformatics, and director of the Center for Advanced Genomic Technology (CAGT), DeLisi leads Boston University’s efforts to understand just how genes regulate the complex folding and unfolding of proteins that control life processes. Under his direction researchers are building systems that simulate cell behavior and shed light on the complex engineering problems involved in controlling that behavior. Working in concert with BU’s Fraunhofer Center for Manufacturing Innovation, and the Departments of Chemistry and Physics, DeLisi’s lab is developing and applying new microarray technologies for fingerprinting the complete molecular state of a cell. These efforts will lead to the development of drugs that can be targeted directly to the site of disease for more effective healing and virtually no collateral damage to adjoining tissue or body systems.

DeLisi is also leading a groundbreaking effort to create “The Virtual Human Project,” a distributed computer program that uses algorithms to re-create the functions of the human body, and in particular to study how functions in one part of the body impact others. Ultimately, the models could predict what a chemical, virus, bacterium, or physical trauma would do at the cell, organ, system, and organism levels. Doctors in an emergency room could see the effects of physical trauma without opening up the body, and patients could have drugs customized to their body chemistry.

To learn more, see www.bu.edu/cagt.

Nanoengineering New Solutions

Biomedical engineer Tejal Desai is in the forefront in developing novel biological microelectromechanical devices (bioMEMS), one of the hottest areas of biomedical engineering research.

Desai is best known for her work designing bioMEMS for treating diabetes. Smaller than half the width of a human hair, the tiny silicon microcapsules designed and built in her lab are filled with insulin-producing pancreatic cells from healthy animals and implanted in the abdomens of diabetic animals. The microcapsules are porous enough to let oxygen and other nutrients flow in to keep the foreign pancreatic cells alive, and let insulin flow out. The openings are small enough, however, that antibodies and white blood cells cannot enter and attack the foreign cells, thus keeping the body’s immune system at bay. This work has the potential to free people with diabetes from multiple daily insulin injections and the often serious consequences of uncontrolled blood-sugar levels.

Desai also is developing a new bioMEMS that would be ingested and travel through a patient’s digestive tract, releasing medication to treat ailments such as intestinal or colon cancer. “It is an oral delivery system that would be intelligent in the sense that it would target a particular part of the body with the peptides and pharmaceutical agents it releases,” she says.

To learn more, see http://bme.bu.edu/faculty/desai.html.
**Deadly Duo**

What do aging and cancer prevention have in common? According to a new study by Barbara Gilchrest, chair of the Department of Dermatology at the Boston University School of Medicine, both result from a mechanism that swings into action when a specific repeated sequence of DNA bases is detected in a cell. Furthermore, according to Gilchrest, researchers may be able to harness this mechanism to create new cancer-prevention strategies.

It is widely known that human cells senesce—they can only divide a limited number of times, about 20 in a healthy adult. This limit is associated with shortening of telomeres—loop-like structures at each end of the central, gene-containing portion of the chromosome. Telomeres, like all DNA, are double stranded, but one strand ends in an overhang normally concealed inside a loop structure. The overhang is composed of the six-base sequence TTAGGG that repeats for a length of approximately 150–200 bases. T, A, and G (thymidine, adenine, and guanine) are three of the four building blocks, or bases, that make up DNA. (The fourth is C, or cytosine.)

The researchers hypothesized that as telomeres shorten in normal aging, or are damaged by other factors such as stress, ultraviolet light, or carcinogens, the overhang sequences are exposed, setting in motion a series of reactions causing the cells to stop replicating, or even to commit suicide (apoptosis). To test this, the researchers introduced small DNA fragments with the same TTAGGG sequence into cells in culture. They observed that the fragments were rapidly taken into the cell nucleus (where the chromosomes are located), and senescence or apoptosis resulted.

“The cell responses were identical to those activated after acute DNA damage or experimental disruption of the telomere loop,” said Guang-Zhi Li, a postdoctoral fellow in dermatology and first author on the study.

“If a cell is at high risk for becoming cancerous because of acute DNA damage or simple aging, which exposes cells to environmental carcinogens over many years, nature wants to protect the tissue,” says Gilchrest. She and her colleagues propose that by triggering DNA damage responses without actually damaging DNA—by providing telomere-mimicking DNA fragments—they may be able to develop new treatments for cancer, a condition in which cells seem to have lost their ability to senesce or otherwise recognize and respond to abnormal DNA. In a series of earlier publications Research Associate Professor Mark Eller, a co-author of the present study, showed that the DNA fragments can stimulate tanning without damaging DNA, and thus protect the skin from sun-induced cancers. Researchers may be able to harness this mechanism to create new cancer-prevention strategies.

**Designing Tissues That Assemble Themselves**

Current methods of tissue engineering rely on seeding mixtures of isolated cells onto a biodegradable scaffold. The addition of growth factors may promote the growth of different types of cells, but generally the resulting tissue contains a limited variety of cells, is relatively flat, and possesses little internal structure. Biologically engineered skin, for example, can be successfully grown by current methods, but functioning kidneys, hearts, and livers cannot.

Joe Tien, another visionary in biomedical engineering, is developing a revolutionary technique for forming complex, three-dimensional tissues that can replace damaged tissue in organs such as the liver, blood vessels, lungs, and brain. Tien’s technique relies on creating small structures built from tiny gel components of various shapes. These are coated on one or more surfaces with thin liquid films. When the gel components are shaken together, they create three-dimensional structures—the pieces are attracted and bound together by capillary action between the coated surfaces. The shapes of the gel components are painstakingly designed so that the assembled final structure resembles the natural structure of the tissue to be replaced. Tien’s research group is currently targeting tissue structures found in the human vascular system and liver.

To learn more, see [www.bme.bu.edu/faculty/tien.html](http://www.bme.bu.edu/faculty/tien.html).

**Cancer’s Environmental Roots**

Researchers at the School of Medicine’s Biochemistry Department are studying how carcinogens and other environmental factors influence the way genes function, causing them to signal cells to reproduce uncontrollably. Professor Gail Sonenshein, whose previous research has indicated that drinking green tea may provide protection against breast cancer, is examining the relationship between environmental factors and three interrelated gene systems that appear to be involved in the onset of breast cancer.

By better understanding the molecular pathways that affect the expression of these genes, Sonenshein and her colleagues hope to pave the way for the creation of biomarkers and powerful new therapies. The multidisciplinary study includes researchers from the School of Medicine’s Department of Medicine, its Department of Pathology and Laboratory Medicine, and the School of Public Health’s Department of Environmental Health.

To learn more, see [www.bu.edu/research/cancer](http://www.bu.edu/research/cancer).
In Joe Tien’s Organogenesis Laboratory, researchers apply techniques from microlithography, self-assembly, microfluidics, and developmental biology to assemble ordered, three-dimensional aggregates of cells that they hope one day soon will replace damaged tissue in complex organs such as lungs and liver.

Model of a tiny dodecahedron gel structure (left) that can be coated on one or more sides to enable it to combine with others and self-assemble into a more complex structure (right).
The Sun’s magnetic field and releases of plasma directly affect Earth and the rest of the solar system. Solar wind shapes the Earth’s magnetosphere and magnetic storms are illustrated here as approaching Earth. The white lines represent the solar wind; the purple line is the bow shock line; and the blue lines surrounding the Earth represent its protective magnetosphere. The magnetic cloud of plasma can extend to 30 miles wide by the time it reaches Earth.

The first picture of the Earth in X-rays was taken in March 1996 with the orbiting Polar satellite. The area of brightest X-ray emission is red. The energetic charged particles from the Sun that cause aurora also energize electrons in the Earth’s magnetosphere. These electrons move along the Earth’s magnetic field and eventually strike the Earth’s ionosphere, causing the X-ray emission.

A solar prominence was recorded by NASA’s SOHO satellite. Energized particles from the Sun released by solar prominences, coronal mass ejections, and solar flares are carried toward Earth by the solar wind, where they interact with the magnetosphere and Earth’s atmosphere to produce space weather.
As the lead institution for a new National Science Foundation Science and Technology Center and a driving force in the exploration and mapping of the Milky Way, Boston University is making valuable contributions to our understanding of the near-Earth environment and the galaxy that we call home.

**Space Weather**

On July 2, 2002, a massive solar eruption, more than 30 times Earth’s diameter in size, blasted away from the Sun. Luckily, the “belch,” which was photographed by the Solar and Heliospheric Observatory (SOHO) satellite, was directed away from our planet. Events such as this occur almost daily when the Sun is active, but most miss Earth. But when a giant, fast-moving cloud of hot gas of this type does buffet the Earth, it can disturb our magnetosphere, disrupting everything from pigeons’ sense of direction to the functioning of telecommunications satellites and power grids.

Space weather can be beautiful—energy carried from the Sun by the solar wind ultimately causes atoms and molecules in Earth’s upper atmosphere to emit light in the form of the aurora borealis. But it can also be devastating. For example, in 1989 a magnetic storm caused massive power outages in Quebec and much of the northeastern United States. In 1998 a solar storm caused a Galaxy 4 satellite failure, disabling 80 percent of the pager systems in the U.S. During the Gulf War, severe ionospheric perturbations significantly degraded communications and navigation by Global Positioning Systems (GPS). Solar activity’s destructive effect has even been cited in the premature ending of the Skylab mission.

As our society grows more reliant on a vulnerable space environment—and more susceptible to disruptions from space weather—it has become economically imperative to forecast these solar storms. The Center for Integrated Space Weather Modelling (CISM) at Boston University, which began operations in August 2002, is a first-of-its-kind consortium that is creating computer models to better predict the potential for solar-storm damage here on Earth. It was established as an NSF Science and Technology Center supported by a $20-million grant for the next five years.

CISM, directed by astronomer W. Jeffrey Hughes, consists of scientists from Boston University, University of California/Berkeley, Dartmouth College, Rice University, Stanford University, the University of Colorado/Boulder, the University of Texas/El Paso, Alabama A&M University, the National Center for Atmospheric Research, the Space Environment Center, and industry interested in space weather research. Other members from the BU Astronomy Department are Nancy Crooker, George Siscoe, and Harlan Spence, chairman of Astronomy. Researchers from other academic departments at BU include Peter Garik from the School of Education, Roscoe Giles, a physicist and computer engineer, and physicist Claudio Rebbi.

For years, space weather forecasters have issued warnings of large magnetic storms whenever they detected a coronal mass ejection (CME) from the Sun. CMEs consist of giant clouds of energetic protons and electrons and strong magnetic fields, traveling from the Sun at up to 2 million miles per hour. Yet, scientists could not tell with any certainty how the CME would affect Earth when it arrived four days later, or whether it would bypass the planet. CISM aims to help forecasters improve the accuracy of space weather predictions by building a physics-based numerical simulation model that describes the space environment between the Sun and the Earth.

Every 11 years, in a predictable cycle, the activity of the Sun increases and becomes patchy and disordered. At high activity, during the so-called solar maximum, there are more CMEs, and a greater chance of solar storms interacting with Earth. That is what happened during the 1989 peak in the solar cycle, when Quebec was plunged into darkness. Even when we are no longer at the peak of a cycle, intense solar activity can still flare up unexpectedly. Such a storm could even put astronauts aboard the International Space Station at risk of radiation poisoning, especially those on a space walk.
With the establishment of space weather models, scientists will be better able to advise power companies when to isolate vulnerable parts of their grid system, when GPS users should switch to alternate navigation systems, when satellites should be shut down, and when astronauts should relocate to safer quarters.

To learn more, see http://www.bu.edu/cism.

**Mapping the Milky Way**

Using the Hubble Space Telescope and other space-based instruments, scientists have produced spectacular images of galaxies millions of light-years from Earth. But, because of Earth’s location about 30,000 light-years out from the center of our home galaxy—the Milky Way—it is difficult to see our own galaxy with such clarity. The problem is akin to that of a bird flying within a large flock. From within the flock it is difficult to see the full flock, but easy to observe the size, shape, and direction of other distant flocks.

At BU’s Institute for Astrophysical Research (IAR), astronomers Dan Clemens, James Jackson, and Thomas Bania have been playing a leading role in the worldwide effort to better visualize and understand Earth’s neighborhood in the larger Universe. They are engaged in several projects, employing different approaches to probe the Milky Way’s properties.

IAR astronomers recently celebrated the mapping of the one-millionth point in the Galactic Ring Survey, a National Science Foundation (NSF) and NASA-funded endeavor that is shedding light on the structure and properties of the Milky Way’s Galactic Ring. First discovered some 25 years ago, this huge structure, known to astronomers as the 5 kpc ring, is rich in molecular gas, making it the dominant star-forming feature of the Milky Way. The survey, led by Jackson, employs the Five College Radio Astronomy Observatory, a radio-telescope sensitive to wavelengths in the mm range, to create detailed maps of the 5 kpc ring. The astronomers expect the data will yield new information about the origin and structure of the ring, the structure of giant molecular clouds and star-formation within them, and the ring’s role in the dynamics, structure, and evolution of our galaxy.

Mimir, a powerful new instrument that Clemens is constructing with funding from NSF, the W. M. Keck Foundation, and NASA, will be used to chart the magnetic fields that lace through the Milky Way. Named after the mythological Norse giant who guards the Well of the Highest Wisdom, Mimir is a wide-field imaging spectrometer and polarimeter that will be used at the Lowell Observatory’s 72-inch Perkins telescope in Flagstaff, Arizona. It senses near-infrared radiation, enabling it to penetrate even into the dense clouds of gas and dust where stars take form, but which are opaque to visible light.

Clemens believes that data collected by Mimir will help clarify the role of magnetic fields in star formation, a question that has eluded scientists up until now because of the enormous difficulty involved in measuring these fields. Mimir may, in fact, shed light on a theory that holds that magnetic fields regulate the speed at which stars form. The theory proposes that without magnetic fields to slow down star formation, the Milky Way would no longer exist—all of its stars would have formed and blazed out of existence eons before man evolved on Earth.

Clemens, Jackson, and Bania are also playing important roles in GLIMPSE (Galactic Legacy Infrared Midplane Survey Extraordinaire), a survey of the Galactic Disk’s mid-infrared radiation. Since much of the mid-infrared can only be detected from above Earth’s atmosphere, the GLIMPSE survey will be performed using NASA’s Space Infrared Telescope Facility, a new space-based infrared observatory launched in late summer 2003.

Jackson is also leading a team proposing to build the Antarctic InfraRed Observatory (AIRO), an infrared telescope optimized for observing large fields of view. AIRO will take maximum advantage of the clear viewing conditions, cold temperatures, and lack of atmospheric distortion in Antarctica to survey vast tracts of the southern heavens.

By analyzing data from these various instruments, the Boston University team seeks to synthesize an accurate picture of our Milky Way Galaxy, and ultimately to understand better the evolution of the Universe.

Boston University’s leadership in Milky Way research was highlighted at the 2003 IAR-hosted international conference, “Milky Way Surveys: The Structure and Evolution of Our Galaxy.” With more than one hundred of the world’s experts in galactic science, this conference brought together the leading theorists on the formation of galaxies with researchers employing the most up-to-date surveying technologies.

To learn more, see http://www.bu.edu/iar.
Astronomer Daniel Clemens is building Mimir, an instrument that will be used with the Lowell Observatory’s 72-inch Perkins telescope to chart the magnetic fields of the Milky Way Galaxy.

The Galactic Ring, currently being surveyed by a team led by BU astronomer James Jackson, is the dominant star-forming area of the Milky Way. The red areas indicate hotter regions where stars are forming, with temperatures dropping off in the green areas surrounding them.
David C. Mountain, a member of the Hearing Research Center, was recently inducted into the American Institute for Medical and Biological Engineering (AIMBE) “for significant engineering-driven advance in the structure-function-mechanism relations of auditory physiology, with emphasis on outer hair cells and cochlea.”
Opening the Doors of Perception

**How we make sense of the world**

What happens between the moment our sensory organs receive stimuli and when our brains comprehend incoming information? And how do we translate those stimuli back to action? Scientists at Boston University are using research methods from disciplines as diverse as computer science, engineering, and neurobiology to reveal how we understand and interact with our environment.

**Modeling How We Hear and Speak**

Boston University’s Hearing Research Center (HRC) brings together an interdisciplinary team of faculty members from six departments and four Schools who study hearing on many levels—mechanisms in the ear, neural networks, and hearing centers in the brain. Through this multifaceted approach they are developing a better understanding of how we hear, and they are creating new approaches to help people who have speech or hearing impairments.

Biomedical engineers Allyn E. Hubbard and David C. Mountain, for instance, develop computational models of various parts of the ear to discover how physical properties and function are related. They are currently investigating the best way for researchers to model the cochlea, the ear’s extremely complex, spiral-shaped inner cavity, where tiny hair cells receive sound waves and relay them to the brain as electrical signals. Hubbard and Mountain also study sound sources and acoustic environments to develop a better understanding of how evolutionary forces have shaped the auditory pathway. They are developing computer simulations of natural environments that will be used to create new models to elucidate the complex functioning of the ear.

In an effort to help improve the design of hearing aids, Gerald Kidd, another HRC member and professor at Sargent College of Health and Rehabilitation Sciences, studies the mechanisms that allow people to focus on certain sounds and tune out others. People who use hearing aids, he says, often find it extremely difficult to distinguish sounds from one another in a noisy environment—even when they are using their aids. Kidd’s research on auditory masking, the process by which sounds interfere with one another, focuses on how the brain identifies sound patterns. His efforts have resulted in a new understanding about how hearing loss impacts a person’s ability to discriminate between sounds and how this is related to the location of the source of sound in space.

It has always been difficult for speech therapists to evaluate people with poor hearing because one vocal aspect—pitch, for instance—can be so extreme that it obscures other problems. But recent research on the perception of speech conducted by Melanie Matthies, another HRC member and Sargent College faculty member, has led to a new diagnostic approach for measuring vocal qualities of the hearing impaired. In 1998, Matthies, working with former BU professor Geoff Platt, developed a method to isolate and measure a variety of vocal qualities, including overall intelligibility, syllabic differentiation, and articulation of vowel and consonant sounds. The approach carefully analyzes how patients read aloud and enables therapists to determine a baseline for treatment and adjust treatment strategies.

Matthies is currently studying how previously deafened people who received cochlear implants perceive speech and how the implant impacts a person’s ability to produce difficult speech sounds. She is also investigating how normal-hearing individuals organize the motor control necessary to produce speech.

To learn more, see http://www.bu.edu/hrc.
James Cherry, director of BU’s Molecular Neurobiology and Behavior Laboratory, studies the cellular mechanisms underlying cognitive and sensory processes. His recent research on a group of enzymes related to dunce, a gene required for learning and memory in the fruit fly, has pointed to its potential role in the processing of odors and pheromones in other animals. Cherry is now conducting experiments on mice to determine how the enzyme group—Type IV phosphodiesterases (PDE4s)—may impact a variety of behaviors, as well as addiction and depression. For more information, see www.bu.edu/psych/faculty/cherry.

Unconscious Learning

Advertisers have long suspected that people are influenced by information they don’t perceive consciously. But recently psychologist Takeo Watanabe demonstrated scientifically that visual learning takes place in the absence of awareness, attention, or even relevance to the task at hand.

Watanabe and his associates in the Vision Sciences Laboratory conducted a series of experiments in which subjects were asked to identify letters on a computer display. In the background the scientists presented a field of randomly moving dots within which a small number of dots moved coherently in one direction, creating a motion signal so weak that it was effectively invisible (exposure phase).

Subjects were tested for their ability to detect coherent motion within a random field of moving dots before and after the letter identification exercise. In the second round of testing, all the subjects were better able to detect motion in the direction of the “invisible” motion that had been presented during the exposure phase. The subjects appear to have learned to detect the direction of motion as a result of frequent exposure, even in the absence of attention or awareness.

A series of follow-up experiments by Watanabe and Aaron Seitz, then a graduate student in the Department of Cognitive and Neural Systems, found that although subliminal, the learning that takes place in such situations is active. In experiments similar to those described above, a “designated direction” was always paired with the targets of the letter-identification task; the other directions were randomly associated with distracters from the letter task.

The researchers found that the subjects’ ability to correctly identify the direction of motion improved only for the “designated direction”—the one that was paired with the correct letter in the identification task, showing that an internal reward can be triggered when a subject successfully recognizes a relevant stimulus. This reward can help the subject learn irrelevant, and even subliminal, information presented at the same time.

“One point of view has been that the eye’s movements are simply noise that gets into the visual processes,” he says, “but our research has shown that the movements are an example of the body’s neural system cooperating with the visual system.”

In addition to revealing the computational principles of human visual perception, Rucci hopes to develop new algorithms in machine vision. For more information, see http://cns.bu.edu/~rucci.
The members of the Center for Memory and the Brain (from left), Michael Hasselmo, John White, Howard Eichenbaum, and Chantal Stern, draw upon psychology, neuroscience, and biomedical engineering to better understand how memory works.

Neurobiologist Helen Barbas studies the prefrontal cortex of primates’ brains to learn more about how behavior arises. This image from her Neural Systems Laboratory at Sargent College reveals prefrontal neurological pathways (excitatory, shown in green) that terminate in a neighboring prefrontal area amidst inhibitory interneurons (red). The interaction between excitatory pathways and inhibitory neurons are one way in which the prefrontal cortex controls behavior.

She studies patients with Parkinson’s disease and HIV who have learning and memory impairment, as well as young and elderly subjects with normal functioning.

Hasselmo’s lab focuses on neurochemicals involved in memory. He and Angel Alonso, a colleague at the Montreal Neurological Institute and McGill University, recently reported in the journal *Nature* convincing evidence that individual neurons in the entorhinal cortex (an area of the brain near the hippocampus) fire single electrical impulses, or spikes, not only when they are activated by sensory input, but for several seconds after sensory input ceases. This sustained neuronal activity indicates working memory, says Hasselmo.

Furthermore, according to Hasselmo, they fire at graded rates. If the neurons begin firing at five spikes per second (five Hz), they maintain firing at five Hz; if additional input pushes them to seven Hz, they maintain a seven Hz level, and so forth. This ability allows the brain to store information about continuous dimensions, a skill needed to keep track of compass headings and distant landmarks as you navigate a kayak, for example.

The researchers are now examining the relationship between sustained neuronal activity and the neurochemical acetylcholine—a substance known to activate neurons but which is depleted in the brains of individuals with Alzheimer’s disease.

White’s lab applies traditional cellular electrophysiological methods and novel approaches from applied mathematics and electrical engineering to understand the molecular and cellular mechanisms by which the hippocampus encodes information about the outside world.

Researchers at CMB hope that a better understanding of the underlying cellular processes of memory and the brain will result in more effective treatments for such brain disorders as Alzheimer’s disease, stroke, and learning disabilities.

For more information, see www.bu.edu/cmb.

Mediating the Sensory/Brain Connection

Neurobiologist Helen Barbas, who holds faculty positions at Sargent College, the School of Medicine, and the Program in Neuroscience, maps the neural pathways in the prefrontal cortex of primates’ brains, the part of the brain that governs much of what defines us as humans. Acting as the central executive of the brain, the prefrontal cortex helps guide behavior, focusing on the task at hand by selecting relevant information arriving from the brain’s sensory systems, and from areas processing memory and emotions.

Malfunction of the prefrontal cortex is implicated in neurologic and psychiatric diseases such as schizophrenia, which partly involves the inability to attach an appropriate emotion to a particular situation. Barbas’s research has led to several important discoveries, including evidence that cognitive and emotional processes are intertwined in the prefrontal cortex and that there is a consistent and predictable pattern in the organization of the pathways. To learn more, see www.bu.edu/mcb/faculty/individual_pgs/barbas.html.

Watching Memory Work

Translating a sentence from an unfamiliar language or figuring a math problem in your head requires working memory—the capacity to keep information in memory while using the information. At Boston University’s new Center for Memory and the Brain, faculty with expertise in psychology, neuroscience, and biomedical engineering are working together to unravel the mysteries of memory.

Howard Eichenbaum, a psychologist and director of the center, studies neuronal activity in the brains of rats as they solve complex problems. “The problem with rats,” Eichenbaum says, “is that I can’t ask them if they remember what they had for breakfast. The beauty of an interdisciplinary center is the cross-pollination of ideas—studies in animals may inspire parallel studies in people and vice versa.”

Among the center’s collaborators are psychologists Chantal Stern and Michael Hasselmo, and John White, a biomedical engineer. Stern uses functional magnetic resonance imaging (fMRI) to examine how the human brain encodes, stores, and retrieves different types of information.
Graduate students Daniel Mocanu (Ph.D., ENG ’03) and Sang Eun Lee (CFA ’04) explore a space weather image on Boston University’s Deep Vision Display Wall.

The simulation was created by researchers at the Center for Integrated Space Weather Modelling (CISM) working with Raymond Gasser from BU’s Scientific Computing and Visualization Group. The Wall is driven by a Linux cluster of dual-processor IBM X330 servers, rendering and manipulating the enormous amounts of data that make up the larger-than-life computer models. The three-dimensional, high-resolution images possible with the Wall allow faculty, staff, and students to better visualize highly complex processes such as space weather, molecular dynamics, and earthquakes.

The Wall is part of a larger computational facility that includes IBM P690 supercomputers, a 52-node Linux computer cluster, as well as the 24-node Linux imaging cluster.

To learn more, see http://scv.bu.edu/Wall/.
Amazing Technologies

Tools for the 21st century

From medicine to transportation, from data management to entertainment—new advances depend on new technologies. Boston University scientists and engineers are in the forefront of developing leading-edge technologies, paving the way for the next generation of products and services.

Building Better Pharmaceuticals

Imagine wanting to learn about something and the only library at your disposal had resource materials limited to topics that began with just a handful of letters—“A,” “B,” and “C,” or “M,” “N,” and “O.” Researchers seeking to find new drugs or understand biological processes are in a comparable situation today. In most cases the chemical “libraries” available to them are severely limited in scope, hampering their efforts to identify just the right chemical to bond with a particular protein to effectively cure a particular disease.

The Boston University Center for Chemical Methodology and Library Development (CMLD), recently established with a $10.7-million “Centers of Excellence” grant from the National Institute of General Medical Sciences of the National Institutes of Health, is poised to help correct this situation.

“This grant,” says Tom Tullius, chairman of the Chemistry Department, “puts Boston University at the forefront of one of the most exciting frontiers of synthetic organic chemistry: the development of new methods to make highly diverse libraries of organic compounds.”

Each “library” is built from a basic chemical structure—often called a “scaffold”—from which thousands of variations are made, each differing slightly from the others as the result of manipulations programmed into the synthesis process. The BU center focuses on asymmetric synthesis of complex scaffolds and molecules that mimic natural products. By coupling compounds together the chemists will generate libraries with unprecedented complexity.

“These chemical libraries,” says John A. Porco, Jr., who directs the CMLD, “are of great interest to pharmaceutical companies in screening for new drugs, as well as to biomedical scientists for use as bioprobes to unravel complex biological processes. The current lack of truly diverse libraries stifies innovation and limits the directions research can take.”

From left, chemists John Porco, Scott Schaus, John Snyder, and James Panek (not pictured), lead BU’s Center for Chemical Methodology and Library Development. The center develops new methodologies to produce novel chemical libraries of small molecules that can be used for biological screening.

To learn more, see www.bu.edu/cmld.
Bright Lights

Finding a suspicious lump is a frightening experience, and the ensuing procedure, a biopsy followed by anxious hours or days of waiting to learn if it is cancer or just a scare, often magnifies the fear. A better way—one that is less invasive and yields immediate results—is being developed by Irving Bigio, an engineer with expertise in biomedical, computer, and electrical engineering.

Bigio, who joined the Boston University faculty in 2001 after more than 25 years at Los Alamos National Laboratory, is working in the realm of biomedical optics—technology that uses light to diagnose and treat disease. Bigio is developing a novel, noninvasive technique that physicians will use to evaluate tumors in the colon, bladder, cervix, or other organs—immediately and without removing tissue. It will also make it possible for surgeons to rapidly determine if they have left any cancerous tissue behind.

Bigio's interest in noninvasive and minimally invasive diagnostics was initially sparked by a call from a gastroenterologist looking for a better way to detect signs of early cancer. The doctor would use an endoscope to examine a patient's colon and do random biopsies—sometimes as many as 30 or 40 on a single patient—and still miss spots of early malignancy. The physician wanted a "magic laser" he could use with an endoscope to pinpoint precancerous or cancerous sites.

Bigio's technique, called optical biopsy, was recently tested for its accuracy in detecting breast cancer. It uses only two thin optical fibers inserted through an endoscope or catheter—one carries light to the surface of the tissue where cancer is suspected, the other relays light scattered back from the tissue to a spectrometer where intensities at different wavelengths are recorded and analyzed on a portable computer. The analysis compares the optical signature of the tissue being tested with known signatures of healthy and cancerous tissue.

In a breast cancer study that was recently concluded, the researchers compared optical measurements with conventional biopsies from more than 200 consenting patients. A random sample of the biopsies was used to "teach" the computer to identify cancer using the optical signatures. The technique was then tested on the remaining biopsies, where it yielded the same diagnosis 93 percent of the time for breast tissue, and 85 percent for lymph nodes.

Bigio and his colleagues at University College, London, are continuing to conduct clinical studies of the optical biopsy system in other tissues. They caution that the results, though promising, are only preliminary, and large-scale tests on many patients will be required before this technology could be available commercially—possibly in three or four years.

Recently inducted into the American Institute for Medical and Biological Engineering (AIMBE), Bigio was cited for outstanding contributions advancing basic theory and practice in biomedical optics, including optical biopsy, interstitial laser thermotherapy, and optical pharmacokinetics.

A Cure for the Synchronization Blues

No longer merely day planners or address books, today's personal digital assistants (PDAs) offer an increasing range of functions, such as multimedia capacity, database software, and Internet access. Doctors use these handheld computers to retrieve medical records and check lab results. Truck drivers turn to their PDAs to communicate with their company, send and receive e-mail, and keep track of expenses, shipping records, maps, and schedules. Even some hunters are known to carry Palm Pilots in the deep woods to help with landmark navigation.

However, as networked and mobile/wireless devices become more complex, they are also proving more difficult to manage. Computer engineers David Starobinski and Ari Trachtenberg, in a project partially supported by the National Science Foundation, are finding new solutions for a growing concern in the industry: the often time-consuming and frustrating process of synchronizing data on PDAs with data on personal computers (PCs).

"At best, conventional synchronization can take a minute or two," says Trachtenberg. "But sometimes it can take up to 20 minutes."
Long synchronization times result from a slow sync algorithm that requires that all the PDA data be transmitted to the PC so the differences between their databases can be determined. This approach is inefficient, say the researchers, because the actual number of differing entries is typically much smaller than the total number of records stored on the PDA. Starobinski and Trachtenberg have proposed, analyzed, and implemented an alternative method, called CPISync (characteristic polynomial interpolation-based synchronization), to speed up the process.

"The most salient property of this scheme is that the amount of communication needed for synchronizing the databases relates only to their mutual differences," says Sachin Agarwal, a graduate student who worked with Starobinski and Trachtenberg on the project. The amount of time the user has to wait depends only on how many changes he makes.

The researchers are now extending CPISync for use in synchronizing multiple computers on a network so that they are all working with the same set of data—a more complex issue since the correct order of synchronization is critical.

Research papers on CPISync were published in the July/August 2002 issue of IEEE (Institute of Electrical and Electronics Engineers) Network Magazine and the January–March 2003 issue of the IEEE Transactions on Mobile Computing.

The Enormous Potential of the Nanoscale

Nanoscale science and technology are expected to change virtually every human-made object within this century. In the 1980s, when researchers first began working at the nanoscale (a nanometer is about 10,000 times smaller than the diameter of a human hair), they were surprised to find that small groups of atoms or molecules often have unexpected properties, such as increased strength, lower electrical resistance, or greater optical absorption. At Boston University the members of the Nanoscience Working Group are collaborating across disciplines to exploit these properties to create new technologies in nano-optics, MEMS (microelectromechanical devices), and bioMEMS (biological MEMS).

With $1.7 million in funding from the National Institutes of Health, an interdisciplinary team led by physicist Bennett Goldberg and electrical and computer engineers Selim Ünlü and Anna Swan is developing a new form of microscopy that will let scientists peer deep inside a living cell, watching as proteins move about doing their work—attaching here, disengaging there. Such a close perspective will enhance our understanding of life’s most basic processes.

Called high-resolution spectral self-interference fluorescence microscopy, the new technique has the potential to produce images of biological phenomena where points as close as a few nanometers apart can be clearly differentiated—a resolution nearly 50 times more powerful than current imaging systems. The key breakthrough was the observation that the interference spectrum created by combining the light emitted upward with that emitted downward from a fluorescent particle, or fluorophore, provides very precise information about its location.

Goldberg and Ünlü are also developing solid immersion lens microscopy, another technique aimed at producing accurate three-dimensional images of nanoscale structures. Funded with a $1.3-million National Science Foundation NIRT (Nanoscale Interdisciplinary Research Teams) grant, the technique utilizes a partial-spherical lens placed directly on the object. Made of a highly refractive material, and embedded with tiny wires, or nano-whiskers, that effectively focus the light energy, these tip-enhanced solid immersion lenses produce high-resolution images of nano-sized structures.

Other members of the Nanoscience Working Group at Boston University, physicists Claudio Chamon and Raj Mohanty, who utilize the recently renovated Nanoscale Research Facility, are working on problems associated with creating quantum nano-junctions. These junctions are crucial if individual nanoscale electronic devices—single electron transistors, quantum dots, nanocrystals, and the like—are to be connected into working devices, such as quantum computers.

Nano-connections are considerably more complex than their counterparts in the micro or millimeter scale. While junctions between larger wires behave predictably as metals with given impedance (resistance), and reflection/transmission coefficients, nanowires such as metallic carbon-nanotubes, behave nonlinearly, and must be understood in terms of quantum mechanics. It is possible, for example, for certain configurations to create repulsive electron interactions that suppress conductance between separately functional units, and create a device that is nonfunctional. Chamon and Mohanty’s research is leading to a better understanding of the nonlinear effects that operate at nano-junctions, work that will ultimately lead to nanoscale devices that operate dependably.

Biomedical engineers Tejal Desai and Joe Tien, among others, are also pushing the boundaries of nanoscale engineering. Read about their work on pages 2–5.
Geologist Andrew Kurtz studies soil samples in the Hawaiian islands, where conditions vary from tropical rain forest to arid desert, and where sites range in age from a few hundred to several million years old. He is interested in the relationships between ecosystems, soil development, and weathering. Noting that soil both loses mass through weathering, and gains mass through deposition of minerals from the atmosphere, Kurtz’s group has found that Asian dust is an important source of phosphorus for the forest ecosystems of Hawaii. This, says Kurtz, illustrates a surprising coupling between climate in Central Asia and the ecosystem of the Hawaiian islands.
Moving Toward Sustainability

How we use and distribute resources

From developing highly efficient fuel cells to prospecting for drinking water with satellites, Boston University researchers are investigating how humans use and distribute Earth’s limited natural resources. Their efforts are revealing new ways to meet the needs of the present without compromising the ability of future generations to meet their own needs.

Changing Climate

Earth scientists at Boston University study the geologic and oceanographic processes that have regulated climate in the past in order to better predict future changes and assess how much of today’s clearly documented global warming is attributable to human intervention as opposed to natural cycles.

These Earth scientists include Maureen Raymo and Andrew Kurtz, who study the role of weathering which removes the greenhouse gas, carbon dioxide (CO₂), from the atmosphere and delivers it to the oceans, where it is ultimately stored in marine sediments. Raymo’s theory, that the cooling of Earth’s atmosphere over the past 40 million years results from enhanced chemical weathering in the mountainous regions of the world, in particular the Himalayas, has been widely accepted. Kurtz’s studies of the links between chemical weathering and the Earth’s carbon cycle are conducted in the Hawaiian islands where the remarkable landscape juxtaposes tropical rain forests with harsh deserts, providing study sites with widely varying rates of precipitation and soil age.

David Marchant’s research in Antarctica addresses global climate change and ice sheet response. Ancient glaciers in the Dry Valleys register temperature and atmospheric evolution over the past eight million years. His data add to our understanding of CO₂ change on million-year time scales and shed light on the future behavior of the East Antarctic ice sheet. By extension to other cold climes, his research, in collaboration with colleagues at Brown University, helps characterize and elucidate the distribution of glacier ice on Mars, providing clues to the variability of the Martian climate.

Rick Murray’s studies of the processes causing changes in biologic productivity in the surface waters of the ocean have demonstrated the intimate association between the oceanic biosphere and climate change. Tiny photosynthesizing plants known as phytoplankton remove CO₂ from the atmosphere and deliver carbon to the deep sediments of the ocean floor. Murray’s research has shown a dramatic increase in such carbon transfer during past glacial periods, when large ice sheets extended over much of the land mass. In related work, Murray and his colleague Terry Plank study the pathways by which iron is picked up from the land, carried through the air on dust particles, and delivered to the ocean. Since iron is required by many marine photosynthesizing plankton, its concentration in seawater is potentially related to the amount of CO₂ that the plankton remove from the atmosphere.

For more information about Earth science, see www.bu.edu/es.

Looking Down from Above

Water may cover 70 percent of the Earth’s surface, but securing sources of potable water in arid regions remains one of the great challenges of the 21st century. A pioneer in the field of remote sensing, Professor Farouk El-Baz is conducting a three-year project for the Sharjah Electricity and Water Authority aimed at locating new sources of groundwater to support the future needs of people in the United Arab Emirates.

El-Baz and colleagues at Boston University’s Center for Remote Sensing are examining images from Landsat 7, one of
NASA’s most recent additions to the fleet of Earth-observation satellites. In a high-tech version of dowsing, the researchers use satellite-based radar to scan below desert sands and locate the beds of former rivers and streams that may still contain groundwater. The team also use instruments that gather different wavelengths of light to identify fracture networks—porous areas in the country’s highlands that are potential reservoirs for groundwater. These techniques were developed and tested by the team in Egypt and Oman to successfully locate underground water.

Geographer Robert Kaufmann also uses satellite images to analyze changing vegetation and land use in the Pearl River Delta of China. Kaufmann has developed econometric techniques to model the demographic and technical factors that influence the rate at which agricultural and natural lands are converted to urban uses. He is using the models to forecast different scenarios for economic development and land use in China.

For more information about the Center for Remote Sensing, see www.bu.edu/remotesensing.

FROM FORESTS TO FIREWOOD

In the Himalayan regions of Nepal and India, wood is the major source of fuel for cooking and heating. Dilip Mookherjee, director of the Institute for Economic Development at Boston University, is studying the factors that influence firewood consumption in villages to better understand the alarming rate of deforestation in these regions.

With data from the World Bank and from his own surveys of over 200 villages, Mookherjee is investigating how households rely on forest products. He is also analyzing state regulation of these products and how the quality and abundance of the tree stock has changed over the last 25 years. Using econometric models, Mookherjee is exploring the impact of poverty, population growth, changing property rights, and economic growth on deforestation.

Mookherjee recently completed an analysis of data from Nepal. The data indicate that if economic development raises living standards without an accompanying increase in educational opportunities, occupational structure, or access to modern fuels, then household energy needs increase and so does the pressure on forests for firewood. His team is currently collecting data in India that will explore these issues in more detail.

IT IS EASY BEING GREEN

Traditionally, corporate behavior regarding the environment weighed profits against social responsibility and found the latter to be expendable. Andrew Hoffman of the BU School of Management, who studies the cultural and institutional aspects of corporate environmental activity, has found that managers acting in the best interest of their investors must consider the environmental impact of their decisions. Banks and insurance companies, for instance, encourage companies to minimize risk by following sound environmental policies. They have found that companies that abide by environmental regulations can avoid costly lawsuits, cleanup fees, and government fines.

For decades, companies have believed that being green is expensive, and that meeting environmental regulations ultimately costs jobs. Economists Linda Bui and Eli Berman, a former colleague now at Rice University, questioned these assumptions by analyzing how environmental regulations on air pollution affect the total productivity of large manufacturing plants in the United States. They focused on oil refineries in the Los Angeles Basin that since 1979 have faced more stringent air quality regulations than those posed nationally. These regulations have forced refineries to use abatement...
technologies that reduce the emission of nitrogen oxides (NOx), sulfurous oxides (SOx), volatile organic compounds (VOCs), and particulate matter (PM10). These substances contribute to the formation of acid rain and, either directly or through the creation of ozone, lead to harmful effects on human health.

Berman and Bui asked whether holding these refineries to a stricter standard of environmental cleanliness negatively impacted the productivity of these companies or forced worker layoffs. They found that, on the contrary, stricter regulation was not responsible for a decline in employment at these oil refineries and that, in fact, they probably increased labor demand and productivity at these plants.

**Food Forecasts**

In Zimbabwe, the production of maize, the country’s primary food staple, is at the mercy of a weather phenomenon halfway around the globe. For decades, scientists have known that El Niño, a disruption in the ocean-atmosphere system in the tropical Pacific, dramatically affects weather patterns around the globe. In strong El Niño years, droughts in southern Africa put the region in danger of famine. With a better understanding of El Niño, scientists now issue seasonal precipitation forecasts to water planners, food security agencies, public health officials, and farmers in Africa. BU geographer Anthony Patt is studying how to communicate these forecasts to subsistence farmers in Zimbabwe in a way they can trust, understand, and use. With advanced warning of an imminent dry season, farmers can plant earlier, use different seed varieties, and withhold fertilizer for a greater yield or a smaller one at reduced cost. Patt has found that the success of the forecasts depends upon the degree to which farmers find the information legitimate, trustworthy, and relevant to their lives.

For more information, see [http://people.bu.edu/apatt](http://people.bu.edu/apatt).

**Green Power: The Promise of Fuel Cells**

Burning coal and oil to generate electricity is undesirable on several fronts. Power plants are the largest source of air pollution in the United States, and they increase American dependence on foreign oil. Engineering faculty members Srikanth Gopalan, Uday Pal, and Vinod Sarin envision a day in the near future when individual homes will manufacture their own electric power with highly efficient solid oxide fuel cells.

Roughly the size of a modern furnace, these devices would supply power to an entire household, eliminating the power grid and the plants we now depend on for electricity. Fuel cells generate electricity through a chemical reaction in which oxygen and hydrogen yield water and heat. Oxygen can be collected from the air, but hydrogen is currently derived from oil and natural gas in an expensive and cumbersome process.

The solid oxide fuel cells that Gopalan and colleagues are developing operate at temperatures close to 1000 degrees Celsius. Gopalan is working on methods to lower the operating temperature of the cells by 100 degrees so that they can be built with less expensive metal alloys, to make them commercially feasible for consumer use. With funding from the U.S. Department of Energy, the team is also developing a ceramic membrane to streamline the conversion of natural gas into hydrogen to fuel the low-temperature cells that are now being developed to power automobiles. One day, according to Gopalan, you may drive up to a pump that uses this membrane and fill your tank—not with gasoline, but with hydrogen.

To learn more, see [www.bu.edu/mfg/grad/green.htm](http://www.bu.edu/mfg/grad/green.htm).

**Assessing Government’s Impact on Quality of Life**

UN Secretary-General Kofi Annan is quoted as saying, “Good governance is perhaps the single most important factor in eradicating poverty and promoting development.”

At Boston University, political scientist John Gerring and political economist Strom Thacker are working toward understanding this relationship—the interplay between national government and the quality of life of its citizens. Their upcoming book, *Good Government: A Global Inquiry*, examines how the strength of national governmental institutions and their constitutional underpinnings relate to the achievement of public interest. They examine the factors that increase state capacity—the ability of public officials to implement a wide range of economic and social public policies—and argue that such capacity is central to a nation’s economic and human development. Gerring and Thacker are currently engaged in research, supported by BU’s Pardee Center for the Study of the Longer-Range Future, that examines the relationship between state capacity and rates of infant mortality.

For more information about the Pardee Center, see [www.bu.edu/pardee](http://www.bu.edu/pardee).
Nelson McNutt, born June 11, 1899, has been gardening at his home in Weston, Massachusetts, since 1939. He shows off his cabbages, tomatoes, strawberries, rhubarb, chard, and morning glories to Thomas Perls, director of BU’s New England Centenarian Study, the world’s largest genetic study of people over the age of 100.
Aging Gracefully
Looking at life at its limits

As the great bulge of the baby boomer generation begins to move into their fifties and beyond, researchers in a wide range of disciplines at Boston University are investigating a multitude of issues to bolster the health, vitality, and quality of life for an aging population.

A History of Service

In 1875, Boston University’s two-year-old School of Medicine launched the Home Medical Service, bringing students to home-bound elderly to provide medical care and other services. Today, assisting more than 600 frail and isolated older adults in the Boston area, this service is only one of a number of significant programs in geriatrics and gerontology at the Medical School. The Gerontology Center, an interdisciplinary center on BU’s Charles River Campus, has prepared students and working adults for careers in elder care since 1974. Another significant center, the Institute for Geriatric Social Work, was recently established with a $4.4-million grant from Atlantic Philanthropies to train social workers and conduct research on issues surrounding geriatric care.

For an overview of geriatrics at the School of Medicine, see www.bu.edu/research/geriatrics. For the Gerontology Center, see www.bu.edu/gerontology. For the Institute for Geriatric Social Work, see http://www.bu.edu/igsw.

Centenarians Yield Secrets of Long Life

When Thomas Perls was a fellow in geriatrics in 1993, he was surprised to find that his two eldest patients were among his healthiest. Both were 100 years old.

“I had been brought up with this idea that the older you get, the sicker you get,” Perls says. “These two centenarians went against the grain.”

Now Perls, an expert on “the oldest old,” as he calls them, directs the largest genetic study of centenarians in the world, the New England Centenarian Study (NECS) at Boston Medical Center, where he is leading a hunt for the secrets of longevity.

By conducting interviews and analyzing genetic material, the researchers are seeking clues as to why such people age slowly and are able to avoid diseases normally associated with aging, such as heart attacks, Alzheimer’s disease, cancer, and stroke.

Recently Perls led a survey of 444 centenarians and their families, which concluded that brothers of centenarians were 17 times more likely to achieve age 100 and sisters were 8 times more likely to reach this age than their counterparts in the general population. At the microscopic level, Perls is examining the genomes of such families, narrowing the search for what he calls a “longevity-enabling gene” that the siblings might share. The discovery of such a gene and the exploration of its biochemical pathways might one day enable development of a drug that mimics its effects, helping older people stave off illness toward the end of their lives.

Perls has a particular interest in Alzheimer’s disease, and has support from the National Institutes of Health and the Alzheimer’s Association’s T.L.L. Temple Foundation Discovery Award for Alzheimer’s Disease Research. He is collaborating closely with the Department of Genetics and Genomics, as well as with specialists from across the disciplines at the Boston University School of Medicine.

To learn more, see www.bu.edu/research/centenarian.

When Seniors Care for Elders

The growth of the elderly population has led to a dramatic rise in the number of informal caregivers — people who provide unpaid help to elders who cannot live independently. The number of such caregivers in the United States rose from an estimated 2.2 million in 1982 to 22 million in 1996. Many of these helpers are themselves elderly persons.

Studies have consistently found that caregivers report higher levels of stress and depression than non-caregivers. An
Aging Gracefully

The unanswered question is whether caregiving has adverse effects on physical health as well. With a $2-million grant from the National Institute on Aging, Lisa Fredman, an epidemiologist at BU’s School of Public Health, is conducting a multisite study of 1,069 elderly women to evaluate what those effects might be. The researchers are compiling data on the incidence of hip fractures and falls, weight change, and other measures of physical functioning.

Fredman and her team screened participants in the Study of Osteoporotic Fractures (SOF), an ongoing, four-site study of elderly American women funded by the National Institutes of Health to find caregivers who were 70 years of age or older. The caregivers and a sample of non-caregivers were interviewed with respect to their physical and emotional health, feelings of stress, and modifiers of stress, such as social support. Additionally, caregivers were asked about their caregiving activities, and stress resulting from these activities. Fredman and her team will reinterview the caregivers and non-caregivers at annual intervals to compare how their physical health changes over time.

Understanding Aging Vision

Psychologist Alice Cronin-Golomb focuses on the effects of visual deficits that accompany increasing age, including those associated with Alzheimer’s and Parkinson’s diseases.

More than four million Americans suffer from Alzheimer’s disease (AD), which brings, along with characteristic memory loss and profound personality changes, increased difficulty in recognizing and discriminating among objects, faces, and patterns. Although part of this difficulty arises from the brain’s impaired ability to process information at a high level, it may also be related to problems in vision itself. Cronin-Golomb and her associates in the Vision and Cognition Laboratory have found that patients with AD are less sensitive to visual contrast, and that creating stronger contrast helps them better recognize objects, read words and letters, and identify faces.

In one study, researchers analyzed food consumption patterns of patients with AD. They found that using red plates, instead of the usual institutional white, made it easier for patients to see the food and substantially increased the amount they ate. This finding may help frail institutionalized people with AD and other dementias eat a more substantial and nutritious diet, an important improvement for people that in general eat far too little.

The researchers also study people with Parkinson’s disease (PD), a severe, progressive neurological disorder that affects between one and one-and-a-half million Americans. These individuals often have multiple problems processing visual information and difficulties in spatial navigation—following street directions, reading maps, and walking a straight line. Cronin-Golomb’s group is collaborating with Robert Wagenaar and colleagues at the human movement sciences group at BU’s Sargent College of Health and Rehabilitation Sciences to examine the direct effect of visual changes on real-world locomotion (see below).

Cronin-Golomb’s research is supported by the National Institute on Aging at the National Institutes of Health and the Alzheimer’s Association.

For further information, see http://www.bu.edu/neuropsychology.

Repairing with Rhythm

People with Parkinson’s disease can often be identified by their characteristic walk, small, shuffling steps, and stiffness in both the upper and lower parts of the body.

In groundbreaking work, Robert Wagenaar, chairman of the Department of Rehabilitation Sciences, physical therapist Terry Ellis, and Ying Hui Chou, a doctoral student at Sargent College’s Center for Neurological Rehabilitation, are investigating new therapeutic interventions for patients with PD that hold promise to restore more normal walking patterns and may help to delay the initiation of intensive regimens of medication and subsequent deterioration in quality of life.

Robert Wagenaar, director of the Center for Neurological Rehabilitation at Sargent College, demonstrates a component of the sophisticated virtual-reality system he and his colleagues developed. It is used to investigate the effects of visual rhythm on movement control and as a therapeutic intervention to improve mobility for patients with Parkinson’s disease.
The researchers observed that while people normally use a variety of gait patterns, shifting patterns seamlessly as their walking speeds up, people with PD seem to be stuck in a single pattern. They are missing the small adjustments in body position that normally occur in response to small changes in the environment. The researchers found that rhythmic stimulation—both auditory (music with a strong beat) and visual (repeating patterns such as stripes on the floor)—helps people with PD increase their ability to walk with more varied gait patterns and at appropriate speeds. Their steps get longer, their pace quickens, and the arms and body move in a more normal fashion.

With support from the National Institutes of Health, and utilizing a sophisticated new virtual-reality system to more precisely control visual effects, the investigators are seeking to learn how to maximize the therapeutic value of rhythmic input for people with Parkinson’s disease, and to understand more about the neurological impact of rhythm on the brain.

Wagenaar and Ellis recently received NIH support to work with occupational therapist Linda Tickle-Degnen to study the efficacy of a self-management rehabilitation program for patients with PD. The researchers will teach individuals with PD to use the rhythmic interventions developed in the clinic at home to help them better manage their disease.

For information about the Center for Neurological Rehabilitation, see www.bu.edu/sargent/neurorehab.

**Bringing Muscle to Bear**

Sargent College of Health and Rehabilitation Sciences is home to a powerful team of researchers who are studying age-related decline in muscle function and developing strategies to prevent some of this loss. Their efforts are directed at understanding what goes on at the level of cells and genes as well as physical changes in muscle and bone.

BU’s Roybal Center for the Enhancement of Late-Life Function, an NIH-funded center working in collaboration with the Robert Wood Johnson Foundation’s Faith in Action program, has launched a nationwide effort to explain the many benefits of staying active late in life and to instruct seniors in how to exercise safely.

Under the direction of Alan Jette, dean of Sargent College, researchers at the Roybal Center have shown that regular, low-impact strengthening exercises significantly increase the strength, mobility, and general health of participating seniors. They have designed an exercise program, Strong for Life, and trained volunteers across the country to teach the exercises to seniors. To learn more, see www.bu.edu/roybal.

Director of Sargent’s Human Physiology Laboratory, Roger Fielding is well known as a pioneer in the study of strength training for the elderly. Currently in the midst of a two-year study funded by the New York City-based Langeloth Foundation, he and his associates are assessing the effectiveness of high-intensity, progressive resistance training in helping stroke survivors regain mobility and other lost functions.

To learn more about the Human Physiology Lab, see www.bu.edu/hpl.

In another study, supported by a Brookdale National Fellowship, the American Federation for Aging Research, and the National Institute on Aging, Fielding compared the effectiveness of power training (quick, explosive bursts of energy to lift heavy weights) to traditional training (slow, deliberate movements, with more repetitions and less weight) in improving functioning of frail older women. He found that traditional training builds endurance and reverses sarcopenia, age-related loss in muscle mass, but power training is more effective in preventing falls, a leading cause of disabling and fatal injuries among the elderly.

In a study led by Susan Kandarian, director of the Muscle Biology Lab, researchers are looking at changes in gene expression that accompany sarcopenia. This two-year study funded by the National Institutes of Health aims first to identify the differences in gene products between the skeletal muscle in older healthy men versus young men. These age-associated differences will provide a standard to assess whether a 12-week weight-training program can reverse or compensate for the aging process.

In a separate study, funded by NASA’s National Space Biomedical Research Institute, Kandarian is looking at the mechanisms underlying muscle protein loss resulting from a sedentary lifestyle, a loss that also occurs during space travel.

For information about the Muscle Biology Lab, see muscle.bu.edu.

**Nutrition, Bones, and Tooth Loss**

Periodontal disease in the elderly often begins with the decline of bone surrounding the teeth. When this alveolar bone wastes away, it can cause teeth to loosen in their sockets, leaving them vulnerable to infections and root caries.

Epidemiologist Elizabeth Krall is exploring theories as to how patients might preserve bone density in this portion of the jaw. She has considered factors that affect bone elsewhere in the body, such as nutrition, hormone replacement, and smoking cessation. In recent studies, funded by the National Institutes of Health and the U.S. Department of Agriculture, Krall and her colleagues gathered strong evidence that calcium and Vitamin D supplements can be useful in slowing the progression of both alveolar bone loss and tooth loss.

Krall’s findings imply that some of the same therapies used to treat or prevent osteoporosis, deterioration of bone in the hips, back, and limbs, might be valuable in combating periodontal disease. Her work deepens our understanding of the ties between oral health and overall health.

For further information, see http://dentschool.bu.edu/research/Health-Faculty/krall.html.
Recent graduate Rahmat Muhammad participated in significant research as an undergraduate with funding from BU’s Undergraduate Research Opportunities Program and an NSF-funded SURF Fellowship. Working with biology department chairman Geof Cooper, she investigated the regulation of a gene that plays a role in controlling the life cycle of cells involved in reproduction and cancer.
A Promising Future

Involving students at all levels

Working side-by-side with some of the world’s foremost researchers—including four Nobel laureates—in the laboratory, in the classroom, and in the field, Boston University students are playing a significant role in producing the new knowledge and technologies that are changing our world.

Probing the Genetics of Birth and Death

Neuroscience and philosophy major Rahmat Muhammad (CAS ’03) became interested in research during her sophomore year at Boston University, after an introductory cell biology class. The experience, she says, left her with questions that she realized could only be satisfied by actively participating in the investigation process.

With a SURF fellowship funded by the National Science Foundation, North East Alliance for Graduate Education and the Professoriate, and administered through the Undergraduate Research Opportunities Program (UROP), Muhammad worked with Department of Biology chairman Geof Cooper. She studied the regulation of c-mos, a gene that is known to be involved in the development of mammalian germ cells (sperm and egg) and is thought to be implicated in certain cancers.

The fact that the c-mos gene is common to many species—including the mouse, humans, and several other vertebrate species—suggests that it is vital to the survival of the organism. It is expressed primarily in germ cells and repressed in somatic cells (all other body cells). Abnormal expression of c-mos in somatic cells, however, generally results either in cell death or in an abnormal proliferation of cells. To prevent this, c-mos must be tightly regulated and restricted to germ cells.

Muhammad investigated the role of COUP-TF (Chicken Ovalbumin Upstream Promoter Transcription Factor) in regulating c-mos. By gaining a better understanding of how c-mos is regulated, she hopes to deepen our understanding of its dual roles in the development of germ cells and cancer.

Muhammad plans to go on to a Ph.D. program in cognitive neuroscience.

Memorable Studies

Sean Wright (UNI ’03), a recent graduate working in the laboratory at psychologist Howard Eichenbaum’s Center for Memory and the Brain, has long been interested in cognitive neuroscience, which integrates the tools and knowledge of such diverse disciplines as psychology, biology, mathematics, computer science, and linguistics to shed light on how we think and learn.

His work in the Eichenbaum lab is helping to develop a better understanding of the mechanisms in the brain that are involved in remembering. Wright’s work focuses on episodic memory—the type of memory for a specific event or sequence of events that helps you remember where you parked your car and the route you drove to get there. He is trying to understand how the hippocampus, a seahorse-shaped structure deep in the brain, facilitates this type of memory.

Wright previously worked on a study in the Eichenbaum lab that established that the hippocampus is essential for rats to make judgments about temporal order (i.e., I went down Park Street before Tremont Street) but is not required for simple recognition (I parked my car on Newbury Street). Wright’s work is aimed at understanding the basis of this difference.

To do this, he presented one group of rats with tests that required them to remember a sequence of movements through a maze (temporal order) and others that only required that they recognize a single odor. After the rats had learned these tasks, Wright measured the levels of c-fos—a gene that is expressed in areas of the brain where cells are actively working. As expected, Wright found higher levels of c-fos expression in the hippocampus region of rats tested for temporal order and in the parahippocampal region of the brain in rats tested for simple recognition.
Wright’s work was presented at the 32nd Annual Meeting of the Society for Neuroscience. It was funded by a grant from UROP. This research also helped him earn a Barry M. Goldwater Scholarship, awarded by the U.S. government to promising scientists, engineers, and mathematicians, a Boston University Harold C. Case Scholarship, and a scholarship from the Scarlet Key Society.

A CLEARER PICTURE

As a graduate student in computer science, Harrison Hong (GRS ’03) studied ways to make the work of radiologists and surgeons easier. Although modern imaging techniques such as CT scans provide very detailed information about internal organs, it remains difficult for physicians to see the information in its complete three-dimensional context. Accurate three-dimensional images would assist them in determining the exact size and precise location of problem areas in organs such as the lungs.

Also, such images would eliminate the need for radiologists to compare repeated studies of internal structures such as pulmonary nodules (growths in the lungs) to determine if a nodule is growing or changing shape and whether it is cancerous or benign.

Hong, a student of computer scientist Margrit Betke, developed a system to precisely align a series of CT images, X-ray-like images taken of multiple slices through the body. This image analysis system begins by segmenting out points on the surface of the lungs and reconstructing them in three dimensions, then anatomical landmarks in consecutive CT scans are used to set up an initial alignment of lung surfaces.

Hong developed a novel, more efficient algorithm to quickly match corresponding lung surface points on the multiple images. This matching process is repeated until the alignment is refined more and more accurately. As the surface points move into better alignment, any nodules within the lung are also automatically aligned, saving radiologists considerable time by not having to match repeated studies manually.

Hong’s and Betke’s work on registration of CT lung surfaces was presented at the Fourth International Conference on Medical Image Computing and Computer-Assisted Intervention, held in Utrecht, The Netherlands, in October 2001. An improved system was presented at the International Conference on Diagnostic Imaging and Analysis (ICDIA) held in Shanghai, China, in August 2002. A paper on the research is scheduled to appear in *Medical Image Analysis* in November 2003.

For more information and images, see www.cs.bu.edu/faculty/betke/research/registration-images.html.
Erin Straw, a participant in the 2002 summer internship program in science, engineering, and mathematics for high school students, working in the laboratory of biologist Ian Callard, where she studied the effects of certain toxins on the reproduction and development of mussels. Callard is interested in invertebrates as bioindicators for potential endocrine, reproductive, and developmental disruption caused by toxic exposure via ground or surface water contamination. Daniel Welty, coordinator of the summer program, looks on.

Cultivating the Next Generation

Boston University faculty and students at all levels are working with pre-college students (kindergarten through grade 12) to build robots, measure light as both a particle and a wave, and solve forensic mysteries by analyzing strands of DNA. By exciting their interest in science and technology, they are paving the way for another generation of young people to focus their intelligence and creativity on solving crucial problems in science and engineering.

A new NSF-funded project known as STAMP (Science Technology and Mathematics Partnerships), led by BU physicist Bennett Goldberg, is creating new partnerships to connect BU faculty and students with classroom teachers (K–12) in four local school systems. They are also drawing on the expertise and resources of some of New England’s most renowned institutions (including the Boston Museum of Science and the New England Aquarium) as well as industry partners. STAMP will work with Boston-area teachers to create innovative programs that support investigation, experimentation, and problem solving in the classroom and laboratory.

STAMP builds upon a number of long-standing programs at the University, under the umbrella of LERNET (Learning Resource Network), that include Mathematics Field Days, Johns Hopkins Center for Talented Youth Events, Engineering Days, Saturday Science Labs, and Weekday Physics Labs, as well as summer internships in science, engineering, and mathematics. LERNET also produces the Pathways Program, one of the first in the nation designed to encourage interaction between young women in high school and female scientists.

To learn more, see www.bu.edu/lernet.
Processing Sound

While locating and identifying the pitch of a sound, in even a chaotic environment, is fairly simple and straightforward for people and animals, producing a sensor that is able to do this is a highly complex engineering problem. Producing a smart acoustic sensor (SAS), based on the human cochlea and smaller than one cubic inch in size, has been the aim of a multidisciplinary team of faculty and students directed by Allyn E. Hubbard, who holds appointments in both biomedical engineering and electrical and computer engineering, biomedical engineer David Mountain, and Tom Bifano, chairman of the department of manufacturing engineering. The collaborators’ efforts earned six students the first-ever collective Dean’s Award from the College of Engineering at Science and Technology Day 2003.

Each of the students contributed to a model or a device crucial to the pathway from sound acquisition (cochlea), to information transmission (auditory nerve), to decoding pitch and location (brain).

Fangyi Chen (ENG ’05), a doctoral student in electrical engineering, helped create a mechanical cochlea that mimics its biological counterpart.

Chen and Shan Lu (ENG ’06), a doctoral student in computer engineering, developed a computational model describing how forces on the outer hair cells of the cochlea generate a slow-travelling pressure wave within the organ of Corti, the part of the cochlea that relays sound information to the auditory nerve.

Electrical engineering doctoral student Zibing Yang (ENG ’04) implemented an advanced version of an electronic cochlea based on an analog microchip that functions as a traveling wave amplifier.

Christian Karl (ENG ’05), a doctoral student in electrical engineering, created a mixed-signal processor, based on a model of the auditory nerve developed in Mountain’s laboratory. The processor can use either the mechanical or the electronic cochlea for input.

Tyler Gore (ENG ’03), who is now working toward his master’s degree in computer systems engineering, Marianne Nourzad (ENG ’08), a doctoral student in computer engineering, and Karl developed both Xilinx and asynchronous VLSI chips which can use the auditory nerve processor described above to extract precise information about the pitch and location of a sound source.

This work was supported by grants from DARPA (Defense Advanced Research Projects Agency). To learn more, see http://www.bu.edu/hrc/. For other research at the Hearing Research Center, see pp. 10–11.
Sponsored Programs Revenue: 1978–2003

Distribution of Research Revenues: 2002/2003

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Sponsored Programs Revenue:
2002/2003 — $311,301,741

FINANCIAL RESOURCES
Endowment: $584.8 million
Total assets: $2.5 billion

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On the Cover
Matthew K. Emsley (Ph.D., ENG ’03) and Yan Li (Ph.D., ENG ’07) work in the Picosecond Spectroscopy and Near-Field Microscopy Laboratories co-directed by physicist Bennet Goldberg and electrical and computer engineer Selim Ünlü. They are working with equipment designed to examine signals from individual quantum dots, an investigation that may someday contribute to the practical development of quantum computing. To learn more about research in the laboratory, see page 17.
The Boston University Medical Campus is home to the BU School of Medicine, the Goldman School of Dental Medicine, the School of Public Health, and Boston Medical Center, as well as BioSquare, a 2.5-million-square-foot biomedical research and business park.